

Complete Summary

GUIDELINE TITLE

Urinary tract infections in renal insufficiency, transplant recipients, diabetes mellitus and immunosuppression. In: Guidelines on the management of urinary and male genital tract infections.

BIBLIOGRAPHIC SOURCE(S)

UTIs in renal insufficiency, transplant recipients, diabetes mellitus and immunosuppression. In: Grabe M, Bishop MC, Bjerklund-Johansen TE, Botto H, Cek M, Lobel B, Naber KG, Palou J, Tenke P. Guidelines on the management of urinary and male genital tract infections. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. p. 52-63. [57 references]

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [July 08, 2008 – Fluoroquinolones \(ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin\)](#): A BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.

COMPLETE SUMMARY CONTENT

**** REGULATORY ALERT ****

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

CONTRAINDICATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES

SCOPE

DISEASE/CONDITION(S)

Urinary tract infection (UTI) complicated by:

- Renal insufficiency (e.g., adult polycystic kidney disease [APCKD], calculi, obstruction)
- Kidney transplantation
- Diabetes mellitus
- Immunosuppression (e.g., human immunodeficiency virus [HIV] infection)

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Nephrology
Surgery
Urology

INTENDED USERS

Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To assist urologists and physicians from other medical specialties in their daily practice
- To provide recommendations on the management of urinary tract infections in association with renal insufficiency, organ transplantation, diabetes mellitus, and immunosuppression

TARGET POPULATION

Patients with urinary tract infections (UTIs) in association with renal insufficiency, organ transplantation, diabetes mellitus, or immunosuppression

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment/Management

1. Antibiotic treatment (e.g., trimethoprim-sulphamethoxazole, co-trimoxazole, fluoroquinolones)
2. Nephroureterectomy or nephrectomy as a last resort
3. Clearance of calculi or other obstruction
4. Stent removal in transplant patients with candidal infection
5. Consideration of drug interactions with cyclosporine and tacrolimus
6. Consideration of drug clearance during dialysis

Prevention

1. Prophylactic antibiotics
2. Treatment of donor kidney
3. Identification and treatment of urodynamic abnormalities before organ transplantation

MAJOR OUTCOMES CONSIDERED

- Morbidity and mortality from complicated urinary tract infection (UTI)
- Recurrence rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

General Search Strategy

Up until 2007, the main strategy was to rely on the guidelines group members' knowledge and expertise on the current literature assuming that all, or almost all, relevant information would be captured.

In updates produced from 2008 onwards, a structured literature search will be performed for all guidelines but this search will be limited to randomized controlled trials and meta-analyses, covering at least the past three years, or up until the date of the latest text update if this exceeds the three-year period. Other excellent sources to include are other high-level evidence, Cochrane review and available high-quality guidelines produced by other expert groups or organizations. If there are no high-level data available, the only option is to include lower-level data. The choice of literature will be guided by the expertise and knowledge of the Guidelines Working Group.

Specific Strategy for This Guideline

For literature review, PubMed was searched for published meta-analyses, which were used as far as available. Otherwise there was a non-structured literature

review process by the group members. Each member was responsible for one chapter (reporter).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomized trials

Ib Evidence obtained from at least one randomized trial

IIa Evidence obtained from at least one well-designed controlled study without randomization

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

III Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

IV Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

General Methods Used to Formulate the Recommendations

- The first step in the European Association of Urology (EAU) guidelines procedure is to define the main topic.
- The second step is to establish a working group. The working groups comprise about 4-8 members, from several countries. Most of the working group members are academic urologists with a special interest in the topic. Specialists from other medical fields (radiotherapy, oncology, gynaecology, anaesthesiology etc.) are included as full members of the working groups as needed. In general, general practitioners or patient representatives are not part of the working groups. Each member is appointed for a four-year period, renewable once. A chairman leads each group.
- The third step is to collect and evaluate the underlying evidence from the published literature.
- The fourth step is to structure and present the information. All main recommendations are summarized in boxes and the strength of the recommendation is clearly marked in three grades (A-C), depending on the evidence source upon which the recommendation is based. Every possible effort is made to make the linkage between the level of evidence and grade of recommendation as transparent as possible.

Specific Methods Used for This Guideline

The members of the Urinary Tract Infection (UTI) Working Group of the European Association of Urologists (EAU) Health Care Office established the first version of these guidelines in several consensus conferences. The members of the current UTI Working Group of the EAU Guidelines Office updated the guidelines in several consensus conferences thereafter. The first draft of each chapter was sent to the committee members asking for comments, which were then considered, discussed and incorporated accordingly.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

- A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
- B. Based on well-conducted clinical studies, but without randomized clinical studies
- C. Made despite the absence of directly applicable clinical studies of good quality

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The formal agreement to each updated chapter was achieved by the European Association of Urology (EAU) working group at three plenary meetings: the first in Paris on 10 December 2004, the next in Istanbul on 15 March 2005, and finally in Florence on 22 October 2005. Each chapter was reviewed by three committee members (editorial group) for consistency and compatibility in two editorial meetings: one meeting took place in Straubing, 22-24 April 2005, and one in Stavern, 9-11 Sept 2005, and the chapters were revised accordingly.

There is no formal external review prior to publication.

The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument was used to analyse and assess a range of specific attributes contributing to the validity of a specific clinical guideline.

The AGREE instrument, to be used by two to four appraisers, was developed by the AGREE collaboration (www.agreecollaboration.org) using referenced sources for the evaluation of specific guidelines. (See the "Availability of Companion Documents" field for further methodology information).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The following is a summary of the recommendations for urinary tract infections in renal insufficiency, transplant recipients, diabetes mellitus, and immunosuppression. Refer to the original guideline for more detailed recommendations and discussion.

Levels of evidence (**Ia-IV**) and grades of recommendation (**A-C**) are defined at the end of the "Major Recommendations" field.

Acute Effects of Urinary Tract Infection (UTI) on the Kidney

In acute pyelonephritis very dramatic changes can occur with focal reduction in perfusion on imaging and corresponding renal tubular dysfunction. However, if in the adult, the kidney is normal beforehand, chronic renal damage is most unlikely. There is no evidence that more prolonged or intensive antibiotic treatment of acute pyelonephritis will shorten the episode or prevent complications.

In diabetes mellitus, overwhelming infection can predispose to pyogenic infection with intrarenal perinephric abscess formation, emphysematous pyelonephritis, and, very rarely, a specific form of infective interstitial nephropathy. Papillary necrosis is a common consequence of pyelonephritis in diabetics. Females are more prone to asymptomatic bacteriuria than diabetic men, but in both sexes progression to clinical pyelonephritis is more likely than in normal individuals. The risk factors for developing asymptomatic bacteriuria differ between type I and type II diabetes.

It is arguable that diabetic patients are susceptible to rapid progression of parenchymal infection. However, the clearance of asymptomatic bacteriuria

should not be attempted if the intention is to prevent complications, notably acute pyelonephritis (**A**).

Chronic Renal Disease and UTI

There are several factors of general potential importance predisposing to infection in uraemia, including the loss of several urinary defence mechanisms and a degree of immunosuppression. Typically, adult polycystic kidney disease (APCKD), gross vesicoureteric reflux (VUR) and endstage obstructive uropathy will harbour infective foci or promote ascending infection, but not invariably so. Clearly, severe UTI with accompanying bacteraemia can hasten progression of renal failure, but there is little evidence that vigorous treatment of lesser degrees of infection or prophylaxis will slow renal functional impairment once it is established (**C**).

In patients with VUR and UTI in endstage chronic renal failure bilateral nephroureterectomy should only be undertaken as a last resort (**B**).

Adult Polycystic Kidney Disease (APCKD)

In patients with acute pyelonephritis and infected cysts (presenting as recurrent bacteraemia or 'local sepsis') treatment requires a long course of high-dose systemic fluoroquinolones, followed by prophylaxis. Bilateral nephrectomy should be utilized as a last resort (**B**).

Calculi and UTI

Management is similar to that for patients without renal impairment (i.e., to clear the stones if possible and to minimize antibiotic treatment if the calculus cannot be removed). Nephrectomy should be performed as a last resort, but even residual renal function may be of vital importance (**B**).

Obstruction and UTI

As in all other situations, the combination of obstruction and infection is dangerous and should be treated vigorously. Obstruction may be covert and require specific diagnostic tests (e.g., video-urodynamics, upper tract pressure flow studies).

UTI in Renal Transplantation and Immunosuppression

The need to correct uropathy or to remove a potential focus of infection in a diseased endstage kidney is more pressing in a patient enlisted for renal transplantation. Even so, the results of nephrectomy for a scarred or hydronephrotic kidney may be disappointing.

Immunosuppression is of secondary importance, although if this is extreme, immunosuppression will promote, at least, persistent bacteriuria, which may become symptomatic. In the context of renal transplantation, UTI is very common, but immunosuppression is only one of many factors which are mainly classified as 'surgical'.

HIV infection is associated with acute and chronic renal disease, possibly through the mechanisms of thrombotic microangiopathy and immune mediated glomerulonephritis. Steroids, angiotensin-converting enzyme (ACE) inhibitors and highly active retroviral therapy appear to have reduced progression to endstage renal disease.

Antibiotic Treatment for UTI in Renal Insufficiency and After Renal Transplantation

The principles of antibiotic treatment for UTI in the presence of renal impairment, during dialysis treatment and after renal transplantation, is discussed in the text (see original guideline document) and summarized in the tables below.

Table: Use of Antibiotics for UTI with Renal Impairment

<ul style="list-style-type: none"> Most antibiotics have a wide therapeutic index. No adjustment of dose is necessary until glomerular filtration rate (GFR) <20 mL/min, except antibiotics with nephrotoxic potential (e.g., aminoglycosides).
<ul style="list-style-type: none"> Drugs removed by dialysis should be administered after a dialysis treatment.
<ul style="list-style-type: none"> Combination of loop diuretics, (e.g., furosemide and a cephalosporin) is nephrotoxic.
<ul style="list-style-type: none"> Nitrofurantoin and tetracycline are contraindicated, but not doxycycline.

Table: Clearance of Antibiotics at Haemodialysis

Dialyzed	Slightly Dialyzed	Not Dialyzed
Amoxycillin/ampicillin	Fluoroquinolones*	Amphotericin
Carbenicillin	Co-trimoxazole	Methicillin
Cephalosporins*	Erythromycin	Teicoplanin
Aminoglycosides*	Vancomycin	
Trimethoprim		
Metronidazole		
Aztreonam*		
Fluconazole*		
<i>*Drugs cleared by peritoneal dialysis</i>		

Table: Treatment of Tuberculosis in Renal Failure

Rifampicin and isoniazid not cleared by dialysis. Give pyridoxine.
Ethambutol not dialyzed. Reduce dose if glomerular filtration rate (GFR)<30 mL/min.
Avoid rifampicin with cyclosporine.

Table: Recommendations for Prevention and Treatment of UTI in Renal Transplantation

<ul style="list-style-type: none"> • Treat infection in recipient before transplantation
<ul style="list-style-type: none"> • Culture donor tissue sample and perfusate
<ul style="list-style-type: none"> • Perioperative antibiotic prophylaxis
<ul style="list-style-type: none"> • 6-month low-dose TMP-SMX (co-trimoxazole) (IbA)
<ul style="list-style-type: none"> • Empirical treatment of overt infection (quinolone, TMP-SMX for 10-14 days)
<i>TMP-SMX = trimethoprim-sulphamethoxazole</i>

Table: Drug Interactions with Cyclosporin and Tacrolimus

Rifampicin
Erythromycin
Aminoglycosides
TMP-SMX
Amphotericin B

TMP-SMX = trimethoprim-sulphamethoxazole.

Definitions:

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomized trials

Ib Evidence obtained from at least one randomized trial

IIa Evidence obtained from at least one well-designed controlled study without randomization

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

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Grades of Recommendation

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- C. Made despite the absence of directly applicable clinical studies of good quality

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for some of the recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of urinary tract infections (UTIs) in association with renal insufficiency, organ transplantation, diabetes mellitus, or immunosuppression

POTENTIAL HARMS

- Antibiotic side effects
- Combination of loop diuretics (e.g., furosemide and a cephalosporin) is nephrotoxic.
- There are important interactions to consider between immunosuppressive agents and antibiotics.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Nitrofurantoin and tetracyclines are contraindicated, but not doxycycline, in patients with renal impairment.
- Nitrofurantoin is contraindicated in newborns.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The purpose of these texts is not to be proscriptive in the way a clinician should treat a patient but rather to provide access to the best contemporaneous consensus view on the most appropriate management currently available. European Association for Urology (EAU) guidelines are not meant to be legal documents but are produced with the ultimate aim to help urologists with their day-to-day practice.
- The EAU believe that producing validated best practice in the field of urology is a very powerful and efficient tool in improving patient care. It is, however, the expertise of the clinician which should determine the needs of their patients. Individual patients may require individualized approaches which take into account all circumstances and treatment decisions often have to be made on a case-by-case basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Association of Urology (EAU) Guidelines long version (containing all 19 guidelines) is reprinted annually in one book. Each text is dated. This means that if the latest edition of the book is read, one will know that this is the most updated version available. The same text is also made available on a CD (with hyperlinks to PubMed for most references) and posted on the EAU websites Uroweb and Urosource (www.uroweb.org/professional-resources/guidelines/ & <http://www.urosource.com/diseases/>).

Condensed pocket versions, containing mainly flow-charts and summaries, are also printed annually. All these publications are distributed free of charge to all (more than 10,000) members of the Association. Abridged versions of the guidelines are published in European Urology as original papers. Furthermore, many important websites list links to the relevant EAU guidelines sections on the association websites and all, or individual, guidelines have been translated to some 15 languages.

IMPLEMENTATION TOOLS

Pocket Guide/Reference Cards

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

UTIs in renal insufficiency, transplant recipients, diabetes mellitus and immunosuppression. In: Grabe M, Bishop MC, Bjerklund-Johansen TE, Botto H, Cek M, Lobel B, Naber KG, Palou J, Tenke P. Guidelines on the management of urinary and male genital tract infections. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. p. 52-63. [57 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Mar

GUIDELINE DEVELOPER(S)

European Association of Urology - Medical Specialty Society

SOURCE(S) OF FUNDING

European Association of Urology

GUIDELINE COMMITTEE

Management of Urinary and Male Genital Tract Infections Guidelines Writing Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: M. Grabe (*Chairman*); M.C. Bishop; T.E. Bjerklund-Johansen; H. Botto; M. Çek; B. Lobel; K.G. Naber; J. Palou; P. Tenke

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Management of Urinary and Male Genital Tract Infections guidelines writing panel have provided disclosure statements of all relationships which they have and which may be perceived as a potential source of conflict of interest. This information is kept on file in the European Association of Urology Central Office database. This guidelines document was developed with the

financial support of the European Association of Urology (EAU). No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance, travel, and meeting expenses. No honoraria or other reimbursements have been provided.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [European Association of Urology Web site](#).

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- EAU guidelines office template. Arnhem, The Netherlands: European Association of Urology (EAU); 2007. 4 p.
- The European Association of Urology (EAU) guidelines methodology: a critical evaluation. Arnhem, The Netherlands: European Association of Urology (EAU); 18 p.

The following is also available:

- Management of urinary and male genital tract infections. 2008, Ultra short pocket guidelines. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. 17 p.

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

PATIENT RESOURCES

None available

NGC STATUS

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Date Modified: 3/2/2009

